

**Stereochemical Control of the DNA Binding Affinity, Sequence Specificity, and
Orientation-Preference of Chiral Hairpin Polyamides in the Minor Groove**

5 The U.S. Government has certain rights to this invention pursuant to Grant Nos.
GM 26453, 27681, and 47530 awarded by the National Institute of Health.

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a continuation-in-part of PCT/US97/03332 filed February 20,
1997, Serial No. 08/853,522 filed May 8, 1997 and PCT/US97/12722 filed July 21, 1997
which are continuation-in-part applications of Serial No. 08/837,524 filed April 21, 1997; *now U.S. Pat. 6,143,901;*
and Serial No. 08/607,078 filed February 26, 1996; *now U.S. Pat. 6,090,947;* and provisional application
60/042,022, filed April 16, 1997 and provisional application 60/043,444 filed April 8,
1997. The specification of these applications are incorporated herein by reference.
Priority is also claimed to provisional applications: 60/023,309; filed July 31, 1996; 60/024,374; filed

BACKGROUND OF THE INVENTION

Field of the Invention

This invention relates to polyamides which bind to pre-determined sites of the
minor groove of double-stranded DNA.

Description of the Related Art

25 The art describes a large variety of polyamides which have three to six
carboxamide base pairs and a hairpin loop derived from γ -aminobutyric acid and the
ability to bind to the minor groove of DNA in the promoter region to inhibit gene
expression. Thus, polyamides consisting of N-methylimidazole (Im), N-methylpyrrole
(Py), and β -alanine and γ -amino butyric acid and methods for preparation of such
polyamides are well known.

30 Polyamides containing N-methylpyrrole and N-methylimidazole amino acids are
synthetic ligands that have an affinity and specificity for DNA comparable to naturally